UNIVERSITY OF PENNSYLVANIA

UNIFICATION OF BROMINATION METHODS OF ANALYSIS AS APPLIED TO PHENOLS AND AROMATIC AMINES

ALLAN R. DAY

A THESIS

IN CHEMISTRY

PRESENTED TO THE FACULTY OF THE GRADUATE SCHOOL IN
PARTIAL FULFILMENT OF THE REQUIREMENTS FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

PHILADELPHIA
1927

UNIFICATION OF BROMINATION METHODS OF ANALYSIS AS APPLIED TO PHENOLS AND AROMATIC AMINES

A THESIS

IN CHEMISTRY

PRESENTED TO THE FACULTY OF THE GRADUATE SCHOOL OF THE UNIVERSITY OF PENNSYLVANIA IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

ALLAN R. DAY

PHILADELPHIA

1927

R. UNIV.
BIBLIOTHEEK
LEIDEN

ACKNOWLEDGMENT

This work was done under the direction of Dr. Walter T. Taggart, to whom the author wishes to express his appreciation for the many suggestions and sincere interest shown throughout the investigation. The author is also greatly indebted to Dr. Ernest C. Wagner for his constructive criticism on various phases of the work.

UNIFICATION OF BROMINATION METHODS OF ANALYSIS AS APPLIED TO PHENOLS AND AROMATIC AMINES

Quantitative bromination, as a method for the determination of phenol, was described by Koppeschaar in 1876.[9] The method is founded upon the fact that in phenol part of the nuclear-hydrogen is readily and definitely replaced by bromine. The way is thus open for analysis, either by weighing the brominated product[1] or by a volumetric determination of the amount of bromine consumed in the bromination. The volumetric method, the one employed by Koppeschaar, is properly called by his name. It is much the more generally useful of the two and is the subject of this paper.

As rapid and definite bromination is more or less characteristic of phenols as a class, and also of many aromatic amines, Koppeschaar's method should be widely applicable to compounds of these types. This was quickly recognized and led to the extension of the method to numerous compounds other than phenol, and to the development of its numerous modifications.

The bromine for the analysis is best supplied by the interaction of potassium bromate and potassium bromide in the presence of sufficient hydrochloric acid to make quantitative the reaction:

$$KBrO_3 + 5\ KBr + 6\ HCl = 6\ Br + 3\ H_2O + 6\ KCl.$$

The bromate is the carefully weighed constituent and determines the amount of bromine liberated. The bromide is simply taken in excess of 5 equivalents, the excess serving both to ensure complete reduction of the bromate and to increase the solvent power of the solution for free bromine.

This device for the liberation of definite quantities of nascent bromine is applied analytically in two familiar procedures: (1) The Excess of Koppeschaar's Method, and (2) The Direct Titration Method.

Many of the procedures suggested since 1876 are apparently hasty adaptations of the direct or excess method to individual

compounds or to mixtures. Often they were developed for technical use and are of doubtful accuracy. It seems very probable that considerable unpublished work on the bromination method must have been done in technical laboratories. The published records of research on the subject are sufficiently voluminous to indicate its importance in organic analysis, but they are surprisingly deficient in two respects: (1) There are relatively few instances in which the investigations were thorough and critical; and (2) there is often a lack of convincing evidence that the compounds analyzed were pure, a lack of definiteness regarding the analytic work itself (e.g., as to the accuracy of the measuring apparatus, standardization of solutions, introduction of the precautions essential to precise iodometric analysis), and a lack of analytical data to indicate properly the accuracy of the results obtained. One of the few exceptions to these statements was the critical and conclusive work of Redman, Weith, and Brock[17] on the analysis of phenol. The fact that a really adequate investigation of Koppeschaar's method as applied to phenol was not made until thirty-seven years after the method was first proposed, gives perhaps a correct idea as to the state of research in this field hitherto. The extensions of the bromination method to compounds other than phenol will be indicated in appropriate places later.

The work to be presented in this paper deals primarily with the excess bromination method and was undertaken in the hope of approaching the following objectives: (1) a simple general procedure applicable, with the fewest possible individual modifications, to the largest number of phenols and aromatic amines; (2) determination of the special deviations from the general procedure necessary to secure accurate analysis of each individual compound; and (3) careful and critical trials of the selected procedures, using carefully purified compounds, accurate measuring apparatus, and using in general a uniform analytical technique, in order to ascertain the merits or demerits of each analysis.

General Procedure for the Excess Method.—A quantity of the substance sufficient for ten analyses is weighed out, dissolved in water, dilute sodium hydroxide (for phenols and sulphonic acids), or dilute hydrochloric acid (for amines), and the

solution diluted to 250 c.c. A 25 c.c. aliquot is pipetted into a 500 c.c. iodine-flask, followed by 25 c.c. of 0.2N "bromine" solution (75 grams of potassium bromide and 5.6 grams potassium bromate per liter), and 50 c.c. of water. Five c.c. of concentrated hydrochloric acid are added and the flask is stoppered at once. It is shaken for one minute and then allowed to stand, with occasional agitation, for a definite interval, which varies with the ease of bromination of the compound analyzed.

The flask is well cooled under the tap or in ice water and 5 c.c. of 40% potassium iodide solution are poured into the trough. The stopper is partly dislodged, whereupon the iodide solution is drawn into the flask with no loss of bromine. The flask is thoroughly shaken, the stopper removed, and the neck of the flask and the stopper washed with water. The free iodine, equivalent to the excess of bromine taken, is titrated with 0.1N thiosulphate, using 5 c.c. of 0.5% starch solution near the end of the titration.

For the blank analyses there are taken 25 c.c. of 0.2N "bromine" solution and 50 c.c. of water, the procedure being otherwise identical with that of the analysis proper.

The expression "general procedure," when used in later pages, refers to the method just described. Any deviations from the conditions specified are noted in the discussion of the individual compounds.

In all cases when the substance is not subject to oxidation, the weight of the sample should be so chosen that a large excess (in general about 100% excess) of bromine will be present. This increases both the rate and the completeness of bromination.

General Procedure for the Direct Titration Method.—This is a general procedure as described by Callin and Henderson.[8] The sample is dissolved as before. A 25 c.c. aliquot is transferred to a beaker, diluted to 200 c.c. and 10 c.c. of a 20 per cent potassium bromide solution are added. It is now acidified with 5–10 c.c. concentrated hydrochloric acid and titrated with a standard potassium bromate solution (0.2N), until a drop of the solution produces a blue spot on starch iodide paper, which persists for 2–4 minutes after the addition of the last drop of the bromate solution. The strength of the bromate solution is determined by titrating the

iodine liberated when 25 c.c. of the potassium bromate solution is acidified with HCl in the presence of 10 c.c. of 20 per cent potassiom bromide solution and 2 grams of iodate-free potassium iodide.

Comments.—The apparent advantages of the direct titration seems to be largely illusory. The use of an outside indicator and the requirement that the final small excess of bromine persist for 2–4 minutes, combine to make the titration unduly tedious. There is, furthermore, some possibility that bromine may be lost, especially near the end of the titration.

Whenever the excess method is applicable, it is preferable. At its best, this method leaves little to be desired as regards accuracy, rapidity, and convenience.

In any bromination method, certain difficulties are introduced by reactions other than those expected. One cause for failure, in a number of cases (e.g., ortho and para toluidines), is the ease with which certain compounds are oxidized by aqueous bromine. This leads to abnormal and indefinite results. It constitutes a limitation upon the applicability of the method, unless the oxidation can be either prevented, as by operating at lower temperatures, or regulated so that the total bromine consumed will still be stoichiometrically related to the compound present. It is hoped in later work to investigate the last-mentioned possibility. Cooling to prevent oxidation has been suggested by Francis.[20] It must be remembered, however, that if the temperature is too low, the velocity of reaction is retarded, making low results possible.

Another difficulty is the precipitation of incompletely brominated products, or the occlusion of unbrominated or partly brominated material by the precipitate. The use of alcohol to prevent precipitation of the brominated product was suggested by Francis[20] for certain compounds. This procedure eliminates the difficulty mentioned, but introduces the complication that alcohol is somewhat attacked by nascent bromine in acid solution. Tests showed that 25 c.c. of a "bromine" solution requiring normally 35.50 c.c. of 0.1N thiosulphate, required 35.30 c.c. after 1 minute in the presence of 25 c.c. of alcohol (at room temperature), 35.15 c.c. after 2 minutes, and only 34.84 c.c. after 5 minutes. Furthermore, duplicate trials for equal periods of

time gave inconsistent results, which seems to exclude the possibility for application of a "correction" for the alcohol.

Other difficulties are met with in certain cases and will be discussed where they occur.

Apparatus and Materials Used.—Each piece of volumetric apparatus was carefully calibrated. The weights used were calibrated by Richard's Method.

The thiosulphate solution was standardized against purified iodine. (Treadwell, 6th edition, 1924, p. 646.) The weighing bottles were put in a desiccator, after adding water to the potassium iodide, and allowed to stand for one hour. They were then transferred to the balance and allowed to stand 15–20 minutes before the iodine was weighed out. (Wagner, *J. I. E. C.*, 16, 617, 1924.)

The bromate-bromide solution was standardized as described in the general procedure. The normality of the two most important solutions was thus based directly and indirectly upon pure iodine.

The phenols and amines used in this work were carefully purified, starting with the best materials obtainable on the market. In a few cases the product was made in this laboratory. Melting points were determined in an apparatus similar to that of Friedrichs (Houben, *Die Methoden der Organischer Chemie*, 3rd Ed., Vol. I, p. 799). Boiling points were determined in an ordinary side-arm distillation flask. The values obtained, suitably corrected, and also the best published values are given in appropriate places below.

Experimental Part

Phenol

The bromination of phenol was first used quantitatively by Landolt,[1] who weighed the precipitated tribromophenol. The volumetric analysis of phenol was initiated by Koppeschaar, using the excess method already outlined. Excess of bromine precipitates tribromophenol hypobromite, which by reducing agents (in the analysis, potassium iodide added to the acid solution) is converted to tribromophenol.

$$C_6H_5OH + 8\ Br = C_6H_2Br_3 \cdot OBr + 4\ HBr$$
$$C_6H_2Br_3 \cdot OBr + 2\ HI = C_6H_2Br_3 \cdot OH + I_2 + HBr$$

One molecule of phenol is thus equivalent to six bromine atoms.

Koppeschaar originally suggested the use either of bromine-water or the bromide-bromate mixture, the latter being, of course, preferable. His published results did not disclose the accuracy of the method, as the trials were made with ordinary carbolic acid.

The method has been studied, modified, and extended by various later workers. It was criticised by Lloyd,[14] who claimed the hypobromite compound to be incompletely reduced on addition of KI. This was disproved by Olivier,[15] who was apparently the first to subject the method to careful trial. He was able to obtain results varying from 99.5 to 99.9 per cent.

Redman and Rhodes[16] and Redmann, Weith, and Brock[17], made a careful and thorough study of Koppeschaar's method and ascertained the conditions most favorable to accuracy, rapidity, and economy. The bromination was found to be complete within one minute, with an excess of only two per cent of bromine over that actually consumed, provided acidity and dilution were properly adjusted. With so small an excess of bromine, the quantity of the relatively costly KI required is inconsiderable. There is claimed for the modified method an accuracy within 0.2 per cent.

After a number of preliminary trials, a procedure closely similar to that of Redman, Weith, and Brock was adopted, with the introduction of several changes designed to eliminate possible errors. The excess of bromine was increased to about 25 per cent (a larger excess is without effect), the time 5–30 minutes. With the minimum excess of bromine and a period of only one minute, the results may be slightly low, as shown in the table below. The more generous conditions provide a greater flexibility and margin of safety.

In the method of Redman, Weith, and Brock, the bromate-bromide solution is added to the acidified phenol solution. Because of the rapidity with which the liberated bromine is substituted in the phenol and of the very slight excess of bromine finally present, there is no loss of bromine.

With the larger excess of bromine, specified above, it is necessary to add the acid last, as stated in the general procedure, to avoid loss of any of the bromine by volatilization before the flask can be stoppered.

Analysis.—The phenol was purified by melting and partial crystallization, until the melting point remained constant at 42.5° (corr.). (I. C. T. gives 41°; Rosenthaler 42.5–43°; Beilstein IV, 40.5–43°.) The general procedure was used. Weight of phenol, 0.5–0.6 gram. Time, 5–30 minutes.

Results.—(*a*) Time, 1 minute; 99.86, 99.89%, mean 99.88%. (*b*) Time, 5 minutes; 99.94, 99.92%, mean 99.93%. (*c*) Time, 30 minutes; 99.94, 99.97, 99.92, 99.92%, mean 99.94%. Four other series, with the same specimen of phenol, gave results varying from 99.82 to 100.01%.

p-Chlorophenol

No record of an analysis of this compound by the excess method was encountered. It was found to present no difficulties. One molecule was equivalent to four atoms of bromine, a dibromochlorophenol being formed.

Analysis.—The p-chlorophenol was purified by fractional distillation, the final melting point being 37.1° (corr.) (I. C. T. gives 37°) and the boiling point 217° (I. C. T. gives 217°). The general procedure was used with little modification. Weight of p-chlorophenol, 0.5–0.7 gram. Water added, 100 c.c. Time, 30 minutes.

Results.—(*a*) 99.92, 99.81, 99.97, 99.92, 99.98%, average 99.89%. (*b*) 99.96, 99.91, 99.80, 99.84, 100.02%, average 99.91%. Two other series gave results varying from 99.79 to 99.95%.

Comments.—Bromination in the smaller volume specified in the general procedure gave lower results. The greater dilution retarded precipitation and apparently rendered bromination quantitative.

Nitrophenols

Vaubel[19] suggested the estimation of o- and p-nitrophenols by the direct titration method, but gave no results. Callin and Henderson[8] determined p-nitrophenol by the direct method,

obtaining results such as 99.92, 99.92 and 100%. Wagner (unpublished data, 1919) analyzed both o- and p-nitrophenol by the excess method and found that quantities from 0.1 gram to a few milligrams could be determined with accuracy. Francis[20] used the excess method, in the presence of alcohol, for the determination of the meta in mixtures containing all the nitrophenols. He gave his mean error, in terms of the meta, as 0.7 per cent. No results were given for the individual compounds.

In the present investigation, it was found that the three nitrophenols can be analyzed by the excess method, using the general procedure. The ortho-isomer brominates less rapidly than the others and in general yields results which are slightly lower than the meta and para. The o- and p-nitrophenols are equivalent to four atoms of bromine, each forming dibrom derivatives. The meta is equivalent to six atoms of bromine, a tribrom derivative being formed.

Analysis of o-Nitrophenol.—The o-nitrophenol was purified by dissolving in alcohol at 35°, adding water at the same temperature and then cooling. After four such crystallizations, the product was crystallized from ether. The melting point was 45.2° (corr.). (I. C. T. gives 45°.) The general procedure was used unchanged. Weight of sample, 0.5–0.7 gram. Time, 30 minutes.

Results.—(*a*) 99.95, 99.81, 99.88, 99.67, 99.74, 99.74%, average 99.80%. (*b*) 99.80, 99.75, 99.90, 99.65, 99.85%, average 99.79%. A third series gave results varying from 99.68–100.16%, average 99.89%; and a fourth result varying from 99.60–99.97%, average 99.78%.

Analysis of m-Nitrophenol.—The m-nitrophenol was purified by repeated crystallization from diluted alcohol at 70°, in the manner outlined above. The melting of the final product was 96.8° (corr.). (I. C. T. gives 96°.) The general procedure was used unchanged. Weight of sample, 0.5–0.6 gram. Time, 5–30 minutes.

Results.—(*a*) 5 minutes: 99.92, 99.87%, mean 99.90%. (*b*) 15 minutes: 99.87%. (*c*) 30 minutes: 99.92, 99.96, 100, 99.87%, mean 99.91%. Three other series gave results varying from 99.81–99.95%.

Analysis of p-Nitrophenol.—The p-nitrophenol was purified by dissolving in sodium hydroxide, boiled with charcoal and filtered. Excess sodium hydroxide was added and the liquid cooled. The separated sodium salt was crystallized from water, dissolved again in water and the phenol precipitated by adding hydrochloric acid. The product was crystallized from 3N hydrochloric acid and finally from water. The melting point was 115° (corr.). (I. C. T. gives 113°; Rosenthaler gives 114°.) The general procedure was used. Weight of sample, 0.7–0.9 gram. Time, 5–30 minutes.

Results.—(*a*) 1 minute: 99.87, 99.87, 99.92, 99.84%, mean 99.87%. (*b*) 5 minutes: 99.92, 99.87%, mean 99.89%. (*c*) 30 minutes: 99.85, 99.76, 99.89, 99.89%, mean 99.85%. Three other series gave results varying from 99.77–99.94%.

Analysis of Mixtures of o-, m-, and p-Nitrophenols for the Determination of the Meta.—The amount of meta may be easily calculated by the solution of simple equations or, as Francis points out, the amount of bromine absorbed in excess of two molecules is a measure of the meta present. If 2.77 molecules of bromine are used, it would indicate the presence of 77% of the meta compound. The general procedure was used. Weight of sample, 0.6–0.7 gram. Time, 30 minutes.

Results.—(*a*) 30 minutes: 49.30, 49.30, 49.22%, mean 49.27%, calculated 49.60%. (*b*) 64.52, 64.71, 64.66, 64.62%, mean 64.62%, calculated 65.07%.

The size of the error seems to increase as the amount of the meta is increased.

2, 4-Dinitrophenol

The bromination of this compound was used quantitatively by Callin and Henderson.[8] They reported that the direct method gave good results.

The excess method, as described in the general procedure, has yielded good results. One molecule of the phenol was equivalent to two atoms of bromine, a monobrom derivative being formed.

Analysis.—The 2, 4-dinitrophenol was purified by repeated crystallization from alcohol. The melting point was 115° (corr.). (I. C. T. gives 111.6°.) The general procedure was used. Sample, 1.5–1.8 grams. Time, 30 minutes.

Results.—(*a*) 99.94, 99.88, 99.94, 100.04%, mean 99.95%. (*b*) 100.10, 99.97, 99.90, 99.97%, mean 99.98%. Two other series gave results varying from 99.80–100.08%.

Hydroxybenzoic Acids

The bromination of salicylic acid was first used, with success, by Freyer,[21] who obtained results varying from 99.5 to 100.95%. He varied the usual excess method by adding the sample to be analyzed last, after the brominating solution had been acidified. Seidell[22] suggested a different procedure as he found Freyer's method unreliable. He used the direct titration method and carried out the bromination in strong hydrochloric acid solution. Under these conditions a dibrom derivative of salicylic acid was formed. The results obtained varied from 98.7–101.8%. Francis[20] applied a modified excess method to a mixture of the three isomers, brominating at −4°. At this temperature the ortho and para isomers formed dibrom derivatives and the meta a tribrom derivative. Francis based upon this behavior a method for determination of the meta acid in the presence of the ortho and para acids, identical in principle with the differential method outlined for the nitrophenols. The average error, in terms of the meta acid, was 1.1%. No results were given for the pure individual acids.

The general procedure, unmodified, gave good results for salicylic acid. The carboxyl group was completely displaced by bromine at 20–25°, with the formation of tribromophenol as the final product, when a large excess of bromine was used. One molecule was then equivalent to six atoms of bromine. The results seem to be of the same degree of accuracy as are obtained by titration with alkali.

Good results were also obtained for the meta acid. The carboxyl group was not displaced, the final product being a soluble tribrom derivative.

Analysis of Salicylic Acid.—The salicylic acid was purified by repeated crystallization from alcohol and finally from water. The melting point was 161° (corr.). (I. C. T. gives 159°.) The general procedure was used. Sample, 0.5–0.6 gram. Time, 30 minutes.

Results.—(*a*) 99.80, 99.89, 99.84%, mean 99.84%. (*b*) 99.84, 99.88, 99.88, 99.92, 99.88, 99.81%, mean 99.87%. Three other series gave results varying from 99.77–99.91%. The same specimen when titrated with standard alkali gave 99.88 and 99.93%.

Analysis of m-Hydroxybenzoic Acid.—The m-hydroxybenzoic acid was purified by repeated crystallization from alcohol. The melting point was 205.2° (corr.). (I. C. T. gives 201.3°.) The general procedure was used. Sample, 0.5–0.6 gram. Time, 15 minutes.

Results.—99.81, 99.90, 99.85, 99.81, 99.77, 99.90%, mean 99.84%. Three other series gave results varying from 99.71–99.92%.

Esters of Salicylic Acid

The ease with which the esters of salicylic acid are hydrolyzed opens the way for their analysis by bromination of the salicylic acid thus obtained. This method was applied with success to methyl salicylate, phenyl salicylate and also to the analogous acetyl salicylic acid. The literature was not found to record any previous similar analyses of these compounds.

Methyl Salicylate

The saponification of this compound by hot dilute alkali is rapid and quantitative. By application of the excess method, the salicylic acid brominates normally.

Analysis.—The methyl salicylate was purified by fractional distillation. The boiling point was 223.5°. (I. C. T. gives 223.3°.) The general procedure was used. Sample, 0.6 gram. Time, 30 minutes.

The hydrolysis was carried out by treating the sample with 5 c.c. of 5% sodium hydroxide. The sodium salt formed was dissolved in a small amount of water and the solution heated just to boiling for ten minutes. The solution was cooled, acidified with hydrochloric acid, made slightly alkaline with sodium hydroxide and diluted to 250 c.c.

Results.—(*a*) 99.99, 99.86, 99.90, 99.81%, mean 99.89%. (*b*) 99.80, 99.84, 99.75, 99.80, 99.84%, mean 99.80%. Five other series gave results varying from 99.75–100.02%.

Phenylsalicylate (Salol)

Emery, Spencer, and LeFebvre[23] applied bromination for the determination of salol mixed with phenacetin. The two were first separated and the salol determined by the excess method; the recovery of salol varying from 98.32–102.3%. Luce[24] described the analysis of salol by Koppeschaar's method in the presen e of alcohol.

Preliminary work proved that the direct bromination of salol was not suitable for analytical work, as the compound undergoes hydrolysis readily. When the sample was hydrolyzed first, the excess method gave good results. After hydrolysis, the reaction consisted of the bromination of a mixture of phenol and salicylic acid. One molecule was thus equivalent to 12 atoms of bromine.

Analysis.—The salol was purified by repeated crystallization from alcohol. The melting point was 43.1° (corr.). (I. C. T. gives 43°.) The general procedure was used. Sample, 0.4–0.5 gram. Time, 30 minutes.

The hydrolysis was carried out by heating the sample, with 100–125 c.c. of 0.N sodium hydroxide, just to boiling for 25–30 minutes.

Results.—(*a*) 99.91, 99.87, 99.95, 99.79, 99.83%, mean 99.87%. (*b*) 99.86, 99.78, 100.00%, mean 99.88%. Three other series gave results varying from 99.77–100.03%.

Acetylsalicylic Acid (Aspirin)

This compound is readily hydrolyzed by dilute acid in the cold. Its analysis by the excess method, therefore, requires no preliminary treatment, as the hydrochloric acid added for liberation of the bromine serves also for the hydrolysis of the ester.

Analysis.—The acetylsalicylic acid was purified by repeated crystallization from alcohol and dried in a vacuum desiccator to prevent any hydrolysis. The melting point was 115° (corr.). (I. C. T. gives 113.5°.) The general procedure was used. Sample, 0.6–0.7 gram. Time, 30 minutes.

Results.—(*a*) 99.93, 99.84, 99.88, 99.80, 99.84, 99.80%, mean 99.85%. (*b*) 99.83, 99.87%, mean 99.85%. (*c*) 99.83, 99.78%,

mean 99.81%. Four other series gave results varying from 99.75–99.94%.

Cresols

Analysis of the cresols by Koppeschaar's method was reported by Ditz and Cedivoda in 1899.[25] Clauser[26] determined the error in the analysis of ortho cresol by bromination to be ±0.5%. Pence[27] was able to determine only meta cresol with accuracy, as the bromination of the ortho and para isomers was accompanied by slow and indefinite replacement of the methyl group by bromine. Redman, Weith, and Brock,[29] in a careful study of the matter, concluded that the bromination methods are uncertain and recommended as preferable the alkaline iodination method. Fox and Barker[30] applied the Koppeschaar method to the determination of meta cresol (equivalent to 6Br) in the presence of the ortho and para isomers (equivalent to 4Br). It was found necessary to use empirical factors for the ortho and para compounds as the use of the theoretical factors produced serious discrepancies. The error in the determination of meta cresol was about 2% when it composed less than 50% of the mixture and 3–4% when more than this was present. Fox and Barker, following Clauser, found the end-point to be improved and the accuracy of the method increased by allowing the analyses to stand for an hour after addition of the iodide, before titrating with thiosulphate. Francis[20] recently modified Koppeschaar's method to permit differential determination of meta cresol in mixtures. His principal innovation was the use of dilute alcohol as a medium for the bromination. The mean error in the determination of meta cresol was 0.6%.

In the present investigation, the excess method has not proven satisfactory for the ortho and para cresols. Various conditions were tried, but the results obtained were not good analytical results and were much affected by analytical conditions. The bromination of the meta proceeded in a more definite manner and good results were obtained. One molecule was equivalent to 6 atoms of bromine.

Analysis.—The m-cresol was purified by repeated fractional distillation. The boiling point was 202.8°. (I. C. T. gives

202.8°.) The general procedure with a few modifications was used. Sample, 0.5–0.6 gram. Time of bromination, 1 minute. Time of standing after the addition of the iodide solution, 60 minutes.

Results.—(*a*) 99.87, 99.71, 100.06%, mean 99.90%. (*b*) 99.68, 99.71, 99.68, 99.75%, mean 99.71%. (*c*) 99.82, 99.82, 99.68, 99.78, 99.58%, mean 99.79%. Three other series gave results varying from 99.65–100.07%.

Comments.—It was found necessary to allow the solution to stand for 60 minutes after the addition of the potassium iodide, otherwise the blue color reoccurred persistently when the liberated iodine was titrated with thiosulphate.

o- and p-Cresols

Good results were obtained for the ortho by direct titration, but comparable results were not obtained for p-cresol.

Analysis of o-Cresol.—The o-cresol was purified by repeated fractional crystallization (see phenol). The melting point was 30.1° (corr.). (I. C. T. gives 30.1°.) The general procedure for the direct method was used. Sample, 1.6–1.8 grams.

Results.—Three series gave results varying from 99.79–100.11%.

Resorcinol

Pence[31] has studied the quantitative bromination of resorcinol very thoroughly. He modified the excess method in several respects: (1) shortened the period of bromination to 1 minute; (2) allowed the solution to stand for 5 minutes after the addition of the iodide; and (3) diluted the solution with 200 c.c. of water before adding the iodide solution, as otherwise a precipitate was formed when the iodide was added.

Good results have been obtained by the method just outlined, but it was found more convenient to dilute the solution before bromination rather than just before the addition of the iodide. A dilution of 100 c.c. was found to be sufficient. One molecule of resorcinol was equivalent to 6 atoms of bromine.

Analysis.—The resorcinol was purified by repeated crystallization from alcohol and finally from water. The melting point was 111.12° (corr.). (I. C. T. gives 110°.) The general procedure

with a few modifications was used. The sample 0.5–0.6 gram was dissolved in water. Dilution, 100 c.c. Time of bromination, 1 minute. Time of standing after the addition of the iodide, 5 minutes.

Results.—100.03, 99.97, 99.95, 100.03, 100.01, 99.95%, mean 99.99%. Three other series gave results varying from 99.89–100.02%.

Naphthols

Vaubel[32] stated that β-naphthol, in acetic acid solution, takes up 1 bromine atom with a sharp end reaction, but no results were given. Seidell[33] used what he termed a new method for β-naphthol, but Elion[34] has established priority, having used the same method much earlier. The method consisted of the determination of the hydrobromic acid formed by the reaction. The results obtained varied from 100.9–103%. Luce[24] used a modified Koppeschaar method for β-naphthol, similar in all respects, except that he used alcohol as a solvent.

The excess method as outlined in the general procedure cannot be used for either of the naphthols in the absence of a solvent. In the presence of chloroform, good results were obtained for β-naphthol, but similar results were not obtained for α-naphthol. The solvent was slightly affected by the bromine, but this was taken care of in the blank determinations. One molecule of β-naphthol was equivalent to 2 atoms of bromine.

Analysis.—The β-naphthol was purified by repeated crystallization from alcohol. The melting point was 123.5° (corr.). (I. C. T. gives 122°.) The general procedure with a few modifications was used. Sample, 1.2–1.5 grams. Solvent, 5 c.c. of chloroform. Time, 15–20 minutes. Dilution, none.

Results.—(*a*) 99.89, 99.82, 100.03, 99.95, 99.76%, mean 99.89%. (*b*) 99.92, 99.75, 99.86, 99.92, 99.75, 99.86%, mean 99.84%. Three other series gave results varying from 99.89–100.02%.

Comments.—It was found best to cool the mixture slightly before acidifying, because of the vapor pressure of the chloroform. The flask should be agitated until the brominated precipitate dissolves in the chloroform. In the titration of the liberated iodine, vigorous shaking was necessary just before the end point was reached, as the chloroform retains the last of the iodine rather tenaciously.

Thymol

Zdarek[35] in 1902 used the excess method for the estimation of thymol. He noted that the blue color returned quickly after the thiosulphate titration, but stated that it should be neglected. The results given varied from 98.6–100.2%. Seidell[36] analyzed thymol by the determination of the hydrobromic acid liberated by the bromination reaction, similar to his determination of β-naphthol. He gave results varying from 99.4–100.7%.

After a number of preliminary trials, it was found that good results could not be obtained in the absence of a solvent. The end reaction was poor and the end point difficult to determine. In the presence of chloroform, the reaction became definite and good results were obtained. One molecule of thymol was equivalent to 4 atoms of bromine.

Analysis.—The thymol was purified by fractional distillation. The melting point was 49.7° (corr.). (I. C. T. gives 51.5°; Mulliken gives 49.6°.) The boiling point was 231.8°. (I. C. T. gives 231.8°.) The general procedure with a few modifications was used. Sample, 0.4–0.8 gram. Solvent, 5 c.c. of chloroform. Dilution, none. Time, 15–20 minutes.

Results.—(*a*) 99.77, 99.68, 99.84, 99.77%, mean 99.76%. (*b*) 99.94, 99.79, 99.86, 99.86%, mean 99.86%. (*c*) 99.89, 99.75, 99.84, 99.65%, mean 99.78%. Four other series gave results varying from 99.64–99.92%.

Comments.—See conditions for analysis of β-naphthol for special conditions.

Aniline

The use of a bromination method for the determination of aniline has been used since 1893 when Reinhardt[37] used the direct method for the analysis of aniline oil. François[38] in 1899 also used the direct method, but used a standard solution of bromine water as the titrating agent. In spite of the frequent use of a bromination method for the analysis of aniline, it has met with criticism at different times. Carson[39] concluded that a bromate-bromide solution, when used directly, does not give accurate or uniform results. Pamfilov[40] also stated that direct titration was not applicable when the concentration of aniline was low.

In the present investigation, it was found that the excess method (general procedure) yielded uniformly excellent results when carried out at a temperature of 10–15°. When carried out at 20–25° some oxidation occurred and the results were high. Under the proper conditions the method leaves little to be desired as to accuracy and convenience. One molecule of aniline was equivalent to 6 atoms of bromine.

Analysis.—The aniline was purified by fractional distillation. The boiling point was 184.5°. (I. C. T. gives 184.4°.) The general procedure was used with little modification. Sample, 0.5–0.6 gram. Temperature, 10–15°. Time, 5–10 minutes.

Results.—(*a*) 99.92, 99.95, 99.92, 99.98, 99.95, 99.92%, mean 99.94%. (*b*) 99.88, 99.88, 99.96, 99.91%, mean 99.91%. Three other series gave results varying from 99.85–99.97%.

p-Chloroaniline

No record of an analysis of this compound by the excess method was encountered. It was found that the excess method yielded good results when carried out at 10–15°. At 20–25° some oxidation occurred and the results were high. One molecule of p-chloroaniline was equivalent to 4 bromine atoms.

Analysis.—The p-chloroaniline was purified by fractional distillation. The melting point was 71.2° (corr.). (I. C. T. gives 71°.) The general procedure was used with little modification. Sample, 1–1.2 grams. Temperature, 10–15°. Time, 10 minutes.

Results.—99.99, 99.96, 100.02, 99.99, 99.93%, mean 99.98%. Three other series gave results varying from 99.85–99.98%.

Nitranilines

Callin and Henderson[8] have determined p-nitraniline by the direct method. The results obtained varied from 99.95–100%. Francis[20] used a modified Koppeschaar or excess method for determination of the meta in mixtures containing the 3 isomers. The o- and p-nitranilines were equivalent to 4 bromine atoms and the meta equivalent to 6. Francis used for the calculation of the meta the same differential method as outlined for the nitrophenols. The analysis was carried out in the presence of alcohol as a special solvent. The mean error, in terms of the

meta nitraniline, was 0.5%. No results for the individuals were reported.

The excess method as outlined in the general procedure gave good results for the ortho and meta compounds. Low results were always obtained for the para, usually from 2–3% too low. The precipitate formed from the bromination of the para was very voluminous and it is probable that some incompletely brominated product was occluded. Various conditions were tried, but none have yielded good results. One molecule of o-nitraniline was equivalent to 4 atoms of bromine and the meta equivalent to 6 atoms.

Analysis of o-Nitraniline.—The o-nitraniline was purified by repeated crystallization from water. The melting point was 71.9° (corr.). (I. C. T. gives 71.5°.) The general procedure was used with little modification. Sample, 0.5–0.6 gram. Dilution, 100 c.c. Time, 30 minutes.

Results.—(*a*) 99.80, 99.80, 99.86, 99.80%, mean 99.81%. (*b*) 99.88, 99.82, 99.95, 99.82, 99.88%, mean 99.87%. Two other series gave results varying from 99.77–99.94%.

Analysis of m-Nitraniline.—The m-nitraniline was purified by repeated crystallization from water. The melting point was 113° (corr.). (I. C. T. gives 111.8°.)

Results.—(*a*) 99.93, 99.98%, mean 99.95%. (*b*) 99.81, 99.90%, mean 99.86%. (*c*) 99.90, 99.95, 99.86, 99.95%, mean 99.91%. Two other series gave results varying from 99.82–99.96%.

Acetanilide

Seidell[41] analyzed acetanilide by the direct method. He hydrolyzed the sample by heating with hydrochloric acid and then determined the aniline set free.

The excess method (general procedure) gave good results when the sample was hydrolyzed before analysis. One molecule was equivalent to 6 atoms of bromine.

Analysis.—The acetanilide was purified by repeated crystallization from alcohol. The melting point was 115.4° (corr.). (I. C. T. gives 114.2°.) The hydrolysis was carried out by heating the sample with hydrochloric acid (5N) just to boiling for

15 minutes. The solution was neutralized with sodium hydroxide and then made slightly acid with hydrochloric acid and diluted to 250 c.c. The general procedure was used with little modification. Sample, 0.5–0.7 gram. Temperature, 10–15°. Time, 5–10 minutes.

Results.—(*a*) 99.80, 99.89, 99.80, 99.84, 99.80%, mean 99.82%. (*b*) 99.80, 99.83, 99.80, 99.86%, mean 99.82%. Three other series gave results varying from 99.79–99.88%.

Aminobenzene-Sulphonic Acids

Callin and Henderson[8] have analyzed sulphanilic acid by the direct method. Their results varied from 100–100.3%. Francis[20] determined the meta in the presence of the para acid. The analysis was carried out at −4°. At this temperature, the para formed a dibrom derivative and the meta a tribrom derivative. The calculation of the meta present was identical in principle with that described for the nitrophenols. No results were given for the individual isomers.

The excess method (general procedure) has yielded good results for the meta and para acids. In the case of the para, the acid group was displaced and tribromaniline precipitated in the presence of a fairly large excess of bromine. The displacement was complete at 15–18°. The meta formed a tribrom derivative but no precipitate.

Analysis of Sulphanilic Acid.—The acid was purified by repeated crystallization from water. The general procedure was used with little modification. Sample, 0.5–0.6 gram. Temperature, 15°. Time, 30 minutes.

Results.—(*a*) 100.01, 99.90, 100.01, 99.95, 100.07, 99.90%, mean 99.97%. (*b*) 99.99, 100.05, 99.99%, mean 100.01%. Three other series gave results varying from 99.88–100.05%.

Analysis of Metanilic Acid.—The acid was purified by repeated crystallization from water. The general procedure was used. Sample, 0.5–0.6 gram. Time, 5–15 minutes.

Results.—(*a*) 99.81, 99.86, 99.75, mean 99.80%. (*b*) 99.80, 99.85, 99.80, 99.74, 99.91, 99.80%, mean 99.81%. Three other series gave results varying from 99.77–99.88%.

Aminobenzoic Acid

Francis[20] applied a modified excess method to mixtures of the 3 isomers. The analysis was carried out at −4°. At this temperature, the ortho and para were equivalent to 4 atoms of bromine and the meta equivalent to 6 atoms. The amount of the meta acid was calculated as described under the nitrophenols.

The excess method (general procedure) gave good results for the ortho and meta acids, but good results were not obtained for the para. o-Aminobenzoic acid formed tribromaniline in the presence of a fairly large excess of bromine, while the meta formed a tribrom derivative, but no precipitate, except on long standing. Instead of getting tribromaniline with the para isomer, an insoluble dibrom derivative was formed, but at the same time some tribromaniline was formed. The results were high based on 4 and low based on 6 bromine atoms. The analysis was attempted at 0°, but the results obtained varied from 97.4–103.8%.

Analysis of Anthranilic Acid.—The acid was purified by sublimation. The melting point was 147° (corr.). (I. C. T. gives 145°.) The general procedure was used with little modification. Sample, 0.5–0.6 gram. Temperature, 15°. Time, 30 minutes.

Results.—(*a*) 99.86, 99.90, 99.86, 99.81%, mean 99.85%. (*b*) 99.80, 99.93, 99.98, 99.86, 99.93, 99.98%, mean 99.91%. Three other series gave results varying from 99.84–99.95%.

Analysis of m-Aminobenzoic Acid.—The acid was purified by sublimation. The melting point was 177° (corr.). (I. C. T. gives 174°.) The general procedure was used. Sample, 0.5–0.6 gram. Time, 10–15 minutes.

Results.—99.80, 99.91, 99.74, 99.80, 99.86, 99.86%, mean 99.83%. Three other series gave results varying from 99.80–100.05%.

Toluidines

Callin and Henderson[8] stated that the direct method was applicable to the toluidines. Francis[20] has determined m-toluidine in mixtures of the 3 isomers. The calculation was based, as usual, on the fact that the o- and p-toluidines were equivalent to 4 bromine atoms and the meta equivalent to 6 bromine atoms. The analysis was carried out at 0°. No results were published

for the individual isomers. The error in terms of the meta varied from .2–1.1%.

The excess method (general procedure) was not applicable to o- and p-toluidines as some oxidation occurred. Results varying from 99.6–100.4% were finally obtained at 0° for p-toluidine, but similar results were not obtained for o-toluidine as other difficulties interfered with the end reaction. In some cases the end point was almost obscured. m-Toluidine offered no such difficulties and good results were readily obtained. The ortho and para toluidines were equivalent to 4 atoms of bromine and the meta equivalent to 6 atoms.

Direct titration was more applicable to the o- and p-toluidines than the excess method, and fairly good results were obtained after a little practice.

Analysis of m-Toluidine.—The m-toluidine was purified by transforming to the hydrochloride, recrystallizing the latter and finally liberating the free base and drying for analysis. The boiling point was 203°. (I. C. T. gives 203.3°.) The general procedure was used with little modification. Sample, 0.5–0.6 gram. Temperature, 10°. Time, 5–10 minutes.

Results.—(*a*) 99.85, 99.81, 99.81%, mean 99.82%. (*b*) 99.85, 99.82, 99.85, 99.85, 99.92%, mean 99.86%. Four other series gave results varying from 99.75–99.96%.

Analysis of o-Toluidine.—The o-toluidine was purified in the same way as the meta. The boiling point was 200.5°. (I. C. T. gives 200.7°.) The general procedure for the direct method was used. Sample, 1.5–1.8 grams.

Results.—The results from 3 series varied from 99.92–100.2%.

Analysis of p-Toluidine.—The p-toluidine was purified by repeated distillation and the crystals formed on cooling were pressed free from the mother liquor. The melting point was 43.6° (corr.). (I. C. T. gives 43.7°.) The general procedure for the direct method was used. Sample, 1.5–1.8 grams.

Results.—The results from three series varied from 99.95–100.3%.

Anisol

The reaction of anisol with bromine was not a definite one. One Br was substituted, but a further reaction occurred, making good results impossible.

Phenolphthalein

In the presence of a solvent, such as $CHCl_3$, phenolphthalein formed a tetrabrom derivative, but in the absence of a special solvent, a yellowish, amorphous precipitate was formed, which corresponded to an absorption of 5 Br. Good results have not been obtained in either case. The results from a large number of analyses varied from 96–103%. Further work may improve these results. The yellowish precipitate lost bromine on standing and a small amount of a crystalline substance was formed by long standing. The reaction is being studied with the hope of identifying the products.

Quinol

Quinol is readily oxidized to quinone by nascent bromine. The quinone reacts with hydroiodic acid with the liberation of an equivalent amount of iodine. An attempt was made to get quantitative results, based on the above reactions, by titrating the liberated iodine with thiosulphate. The results were not consistent and the blue color persistently reoccurred. It is probable that the difficulty arises from the reversible reactions

$$\text{Quinol} \underset{\text{HI}}{\overset{\text{I}_2}{\rightleftharpoons}} \text{Quinone.}$$

Rzymkowski has determined quinone by direct titration with thiosulphate (Z. Elektrochem, *31*, 371, 1925). The quinone acts directly with the thiosulphate, the final reactions being represented by the equation—

$$2\ C_6H_4O_2 + 4\ H^+ + 2\ S_2O_3 = C_6H_2(OH_2)(S_2O_3H)_2 + C_6H_2(OH)_2.$$

It may be possible in later work to determine quinone, formed from quinol, by this reaction. Preliminary work has yielded results with an error of about 2%.

Dimethylaniline

High results were obtained with this compound by the excess method. Two Br atoms were substituted in a short time, but the reaction proceeds further. According to Callin and Hender-

son,[8] this compound may be determined by direct titration at an elevated temperature with the absorption of 3 Br.

Benzidine

A definite substitution apparently occurred, but due to oxidation, which readily occurs, good results have not been obtained.

Arsanilic Acid

The acid group was readily displaced by Br with the formation of tribromaniline, but good results have not been obtained. The action of H_3ASO_4 and H_3ASO_3 on HI and I_2 probably accounts for the fact that the end reaction was not well defined.

Carbazol

A definite substitution apparently occurred, but low results have been obtained in all cases (96–97%). It has been very difficult to find a suitable solvent for this substance. With a suitable solvent, the results would become much better. Further work may overcome this difficulty.

SUMMARY

1. The excess bromination method or Koppeschaar's method has been used for the analysis of a number of Phenols and Aromatic Amines. A general analytical procedure for this method has been worked out, which is applicable, with few modifications, to a great many compounds.

2. Greater care was taken in the purification of the substances to be analyzed than in most of the previous work, thus making possible a more accurate interpretation of the value of the method.

3. Good results were obtained for phenol, o-, m-, and p-nitrophenols, 2, 4-dinitrophenol, p-chlorophenol, salicylic acid, m-hydroxybenzoic acid, methylsalicylate, acetylsalicylic acid, phenylsalicylate, m- and o-cresols, resorcinol, β-naphthol, thymol, aniline, p-chloroaniline, o- and m-nitranilines, acetanilide, sulphanilic acid, metanilic acid, anthranilic acid, m-aminobenzoic acid, and o-, m- and p-toluidines.

4. In all cases (with the exception of phenol, p-nitrophenol, o-, m-, and p-cresols, resorcinol, p-nitraniline and the toluidines), (*a*) better results have been obtained than in any previous published work, and (*b*) the method has been extended to include p-chlorophenol, methylsalicylate, phenylsalicylate, acetylsalicylic acid and p-chloroaniline.

5. The excess method, as compared with the direct titration method, is to be preferred when applicable. The direct method is tedious and desirable only when the excess method cannot be used.

LITERATURE

[1] Landolt, *Ber. d. Chem. Ges.*, *4*, 770, 1871.
[2] Chabrie, *Rev. Chim. Anal. Appl.*, *6*, 138, 1898.
[3] Autenrieth and Beuttel, *Archiv. der Pharm.*, 112, 1912.
[4] Degener, *J. Pr. Ch.*, *17*, 390, 1878.
[5] Waller, *Chem. News*, *43*, 152, 1881.
[6] Seubert, *Ber. d. Chem. Ges.*, *14*, 1581, 1881.
[7] Telle, *Chem. News*, *83*, 51, 1901.
[8] Callin and Henderson, *J. S. C. I.*, *41*, 161, 1922.
[9] Koppeschaar, *Zeit. Anal. Ch.*, *15*, 233, 1876.
[10] Weinreb and Bondi, *Monat. f. Ch.*, *6*, 506, 1885.
[11] Toth, *Zeit. Anal. Ch.*, *25*, 160, 1886.
[12] Beckurts, *Zeit. Anal. Ch.*, *26*, 391, 1887.
[13] Stockmier, *Chem. Ztg.*, *17*, 119 and 131, 1893.
[14] Lloyd, *J. A. C. S.*, *27*, 16, 1905.
[15] Olivier, *Rec. Trav. Chim.*, *28*, 354, 1909.
[16] Redman and Rhodes, *J. I. E. C.*, *4*, 655, 1912.
[17] Redman, Weith, and Brock, *J. I. E. C.*, *5*, 389, 1913.
[18] Versfeld, *Analyst*, *40*, 281, 1915.
[19] Vaubel, *J. Pr. Ch.*, *49*, 540, 1884.
[20] Francis, *J. A. C. S.*, *46*, 2498, 1924.
See also *J. A. C. S.*, *48*, 1631, 1926, "Relative Velocity Constants of Bromination."
[21] Freyer, *Chem. Ztg.*, *20*, 820, 1896.
[22] Seidell, *J. A. C. S.*, *31*, 1168, 1909.
[23] Emery, Spence, LeFebvre, *J. I. E. C.*, *7*, 681, 1915.
[24] Luce, *Ann. fals.*, *16*, 293, 1923; *Repert. Pharm.*, *35*, 42, 1924.
[25] Ditz and Cedivoda, *Zeit. Angew. Ch.*, 873, 1899.
[26] Clauser, *Osterr. Chem. Zeit.*, *2*, 585, 1900.
[27] Pence, *J. I. E. C.*, *4*, 518, 1912.
[28] Autenrieth and Beuttel, *Archiv. der Pharm.*, 112, 1910.
[29] Redman, Weith, and Brock, *J. I. E. C.*, *5*, 831, 1913.
[30] Fox and Barker, *J. S. C. I.*, *169*, 1920.
[31] Pence, *J. I. E. C.*, *3*, 820, 1911.
[32] Vaubel, *Zeit. Anal. Ch.*, *35*, 164, 1896.
[33] Seidell, *A. C. J.*, *43*, 508, 1912.
[34] Elion, *Rec. Trav. Chim.*, *7*, 211, 1888.
[35] Zdarek, *Zeit. Anal. Ch.*, *41*, 227, 1902.
[36] Seidell, *J. Wash. Acad. Sci.*, *1*, 196, 1911.
[37] Reinhardt, *Chem. Ztg.*, *17*, 413, 1893.
[38] François, *J. Pharm.*, *9*, 521, 1899.
[39] Carson, *J. I. E. C.*, *17*, 62, 1925.
[40] Pamfilov, *J. I. E. C.*, *18*, 763, 1926.
[41] Seidell, *J. A. C. S.*, *29*, 1091, 1907.

Other References

Benedikt, Ann., *199*, 127, 1879. First mention made of tribromphenolbrom.
Thiele and Eichwede, Ber., *33*, 673, 1900. Structure of tribromphenolbrom.
Lauer, *J. A. C. S.*, *48*, 442, 1926. Structure of tribromphenol-bromide.